REMARKS

Claim 1 has been amended to limit the hydrophilic polymer to a hydrophilic polymer selected from polyvinylpyrrolidone, polyethylene glycol, polypropylene glycol, polyvinyl alcohol, polyethyleneimine, polyallylamines, polyvinylamine, polyacrylic acid, polyacrylamide, and copolymers and graft polymers of these. This amendment is supported in the specification of the present application on page 15, lines 17-22.

Claim 16 has been amended to limit the hydrophilic polymer to polyethylene glycol.

Referring to the Action, all of the claims are rejected under 35 U.S.C. § 103(a) as being unpatentable over a combination of references. Claims 1-5, 7-17 [sic? 7, 9-17] and 40 are rejected over Kasai et al., US 4,776,959 ("Kasai"), in view of Shimagaki et al, US 5,938,929 ("Shimagaki"). Claim 6 is rejected over Kasai in view of Shimagaki in further view of Graiver et al., US 5,429,839. Claim 8 is rejected over Kasai in view of Shimagaki in further view of Nagatomo et al., US 5,023,052. Claim 12 is rejected over Kasai in view of Shimagaki in further view of Ricketts et al., US 2,715,091.

Kasai is identified by the Office as disclosing a modified substrate which meets each of the limitations of the claims except

that Kasai does not disclose a hydrophilic polymer covalently bonded to a substrate. In Kasai, a water-insoluble hydrophilic polymer is coated on the pores of a hydrophobic membrane. The Office notes that the hydrophilic polymer in Kasai includes vinyl alcohol-vinyl acetate copolymer and that Kasai in Col. 6, lines 38-42, discloses that, optionally, the vinyl alcohol-vinyl acetate copolymer may be cross-linked and further insolubilized.

Shimagaki is cited as teaching that irradiating a substrate with radiation results in covalent bonding as well as crosslinking.

The position of the Office is that it would have been obvious to substitute the process of crosslinking taught by Shimagaki for the crosslinking process as disclosed by Kasai "to provide an insoluble hydrophilic polymer on a hydrophobic membrane substrate thereby providing safety of the product when used for medical purposes." (Action, page 4, lines 6-8 from the bottom of the page).

Applicants respectfully request reconsideration and removal of the 35 U.S.C. § 103(a) rejections. A person of ordinary skill in the art would not have been motivated to combine Kasai and Shimagaki as proposed by the Office. Moreover, even if combined as proposed by the Office, the combination of Kasai and Shimagaki fails to support a case of prima facie obviousness of independent

claims 1 and 16 and the claims that depend thereon.

First, a person of ordinary skill in the art would not have been motivated to combine Kasai with Shimagaki as proposed by the Office to "provide an insoluble hydrophilic polymer on a hydrophobic membrane substrate" because the hydrophilic polymer of Kasai is different from that of Shimagaki (and that of the present invention). Specifically, the hydrophilic polymer of Kasai is originally a water-insoluble hydrophilic polymer as clearly described in Kasai. Because the hydrophilic polymer of Kasai is originally water-insoluble, there is no need to use gamma ray irradiation to make the hydrophilic polymer water-insoluble. On the other hand, the hydrophilic polymer of Shimagaki (and that of the present invention) is water soluble. It is essential for such a water-soluble hydrophilic polymer to be covalently bonded to the surface of the precursor substrate by gamma ray irradiation to make the hydrophilic polymer water-insoluble.

Furthermore, even if Kasai and Shimagaki were hypothetically combined, the modified substrate of the present invention would not be obtained. Although gamma ray irradiation is essential for bonding a hydrophilic polymer to the precursor substrate, gamma ray irradiation also causes degradation of the hydrophilic polymer. Such degradation decreases hematologic compatibility of the

obtained modified unless an antioxidant is used. (Specification, page 19, line 24, to page 20, line 11). As exemplified in Example 1 and Comparative Example 1 of the present invention, if gamma ray irradiation is carried out without an antioxidant, the obtained modified substrate will have a number of adhered human blood platelets larger than $10/4.3x10^3$ μm^2. Because neither Kasai nor Shimagaki discloses use of an antioxidant, a modified substrate obtained by combining Kasai and Shimagaki as proposed by the Office will have a number of adhered human blood platelets larger than $10/4.3x10^3$ μm^2.

The Office states on page 5 of the Action that heparin will minimize the number of adhered human blood platelets. However, when hematologic compatibility of the obtained modified substrate is low, such as in the Comparative Examples of the present invention, the number of adhered human blood platelets is larger than $10/4.3x10^3$ μm^2, despite the existence of heparin. Therefore, the assertion of the Office, which is not supported by any evidence, is not based on a proper technical foundation.

Regarding claim 16, the claim includes the same limitation of number of adhered human blood platelets as claim 1. Therefore, claim 16 is patentable for the same reasons as explained above with respect to claim 1.

Furthermore, regarding the polymethyl methacryrate substrate of claim 16, Kasai describes that polymethyl methacryrate can be incorporated into polyvinylidene fluoride. However, in Kasai major component is polyvinylidene fluoride and polymethyl methacryrate is a minor component, while in the invention of claim 16 polymethyl methacryrate is a major component.

The modified substrate of the present invention, as described in the specification on page 11 lines 14-17, can unexpectedly achieve high hematologic compatibility while maintaining the adsorption of a cytokine such as IL-6. Polymethylmethacrylate is particularly preferable for the precursor substrate when the substrate is used as a medical substrate for adsorbing and removing a cytokine such as IL-6 (specification, page 15, lines 4-9). The reason for this preference is that although the hydrophilization treatment performed on the surface of the substrate causes the adhesion on the substrate of blood platelets or proteins related to clotting to be suppressed, at the same time, the adsorption on the substrate of target substances to be removed such as IL-6 is also suppressed. However, applicants discovered that the combination of polymethylmethacrylate and polyethylene glycol can achieve both suppression of adhesion on the substrate of blood platelets and high adsorption of IL-6 at the same time.

The hydrophilic polymer is limited in claim 16 to polyethylene glycol. Kasai does not disclose the combination of polymethylmethacrylate and polyethylene glycol. Kasai only describes that polymethyl methacryrate can be incorporated as a minor component in the substrate. And Kasai does not disclose polyethylene glycol. Kasai discloses a block copolymer containing an ethylene glycol component, but the copolymer is not a polyethylene glycol.

Kasai, of course, is silent regarding the unexpected results obtained by the combination of polymethylmethacrylate and polyethylene glycol. Shimagaki is also silent with respect to such results. Therefore, even if Kasai and Shimagaki are combined, the modified substrate of claim 16 is not obtained.

For the above reasons, claims 1 and 16 are patentable under 35 U.S.C. § 103(a) over the combination of Kasai and Shimagaki. Removal of the 35 U.S.C. § 103(a) rejection of claims 1-5, 7-17 [sic? 7, 9-17] and 40 is in order.

The remaining 35 U.S.C. § 103(a) rejections depend on the propriety of the 35 U.S.C. § 103(a) rejection of claim 1 on which the rejected claims depend. Since claim 1 is patentable under 35 U.S.C. § 103(a), the claims dependent on claim 1 are prima facie patentable. Removal of the remaining 35 U.S.C. § 103(a) rejections

is also in order.

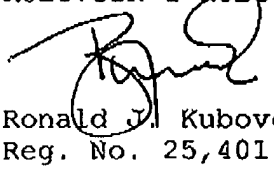
The foregoing is believed to be a complete and proper response to the Office Action dated October 15, 2009.

In the event that this paper is not considered to be timely filed, applicants hereby petition for an appropriate extension of time. The fee for any such extension may be charged to our Deposit Account No. 111833.

In the event any additional fees are required, please also charge our Deposit Account No. 111833.

Respectfully submitted,

KUBOVCIK & KUBOVCIK



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